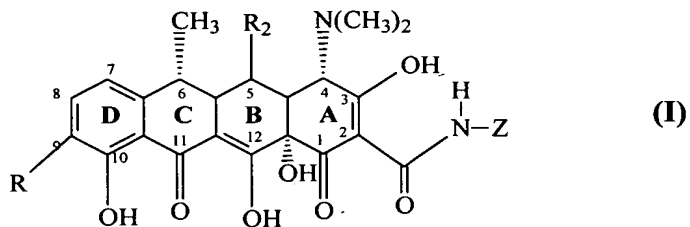


Claims*What is claimed is:*

1. A 5,9-substituted tetracycline.
2. A compound of claim 1 of the following Formula I:



wherein R is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

R² is alkanoyl; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or heteroaromatic group; and pharmaceutically acceptable salts thereof.

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3. A compound of claim 1 that is
- 5 5-propionate-9-t-butyl doxycycline;
9-chloro-t-butyl-5-propionate doxycycline;
9-t-butyl-6-alpha-deoxy-5-oxy-tetracycline;
9-t-butyl-5-oxytetracycline;
9-t-butyl-6-alpha-deoxy-5 -formyloxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-acetoxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-propionyloxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-phenylcarbonyloxy-tetracycline;
10 9-t-butyl-6-alpha-deoxy-5-benzylcarbonyloxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-dimethylaminocarbonyloxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-cyclopentylcarbonyloxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-cyclobutylcarbonyloxy-tetracycline;
9-t-butyl-6-alpha-deoxy-5-cyclohexylcarbonyloxy-tetracycline;
15 9-t-butyl-6-alpha-deoxy-5-cycloheptylcarbonyloxy-tetracycline;
9-(chloro-t-butyl)-6-alpha-deoxy-5-oxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
9-(amino)-t-butyl-6-alpha-deoxy-5-oxy-tetracycline;
9-[(piperidino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
20 9-[(diethylamino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
9-[(dipropylamino)-t-butyl]-6-alpha-deoxy-5-oxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-formyloxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-acetoxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-propionylcarbonyloxy-tetracycline;
25 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-phenylcarbonyloxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-benzylcarbonyloxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-dimethylaminocarbonyloxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclopentylcarbonyloxy-tetracycline;
30 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclobutylcarbonyloxy-tetracycline;
9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclohexylcarbonyloxy-tetracycline; or
35 9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cycloheptylcarbonyloxy-tetracycline; and pharmaceutically acceptable salts thereof.

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4. The compound of claim 2 wherein R is alkyl having 1 to about 20 carbon atoms; alkenyl having 2 to about 20 carbon atoms; alkynyl having 2 to about 20 carbon atoms; alkoxy having 1 to about 20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1 to about 20 carbon atoms; or aryalkyl;

R^2 is alkyl having 1 to about 20 carbon atoms; alkenyl having 2 to about 20 carbon atoms; alkynyl 2 to about 20 carbon atoms; alkoxy 1 to about 20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1 to about 20 carbon atoms; or aryalkyl; alkanoyl from 1 to about 20 carbon atoms; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic; and

Z is hydrogen, alkyl having 1 to about 20 carbon atoms; alkenyl having 2 to about 20 carbon atoms; alkynyl 2 to about 20 carbon atoms; alkoxy 1 to about 20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1 to about 20 carbon atoms; aryalkyl; carbocyclic aryl, or an heteroalicyclic group.

5. The compound of claim 2 wherein R is alkyl having 1 to about 12 carbon atoms; alkenyl having 2 to 12 about carbon atoms; alkynyl having 2 to 12 about carbon atoms; alkoxy having 1 to about 12 carbon atoms; alkylthio having 1 to about 12 carbon atoms; alkylsulfinyl having 1 to about 12 carbon atoms; alkylsulfonyl having 1 to about 12 carbon atoms; alkylamino having 1 to about 12 carbon atoms; or benzyl;

R^2 is alkyl having 1 to about 12 carbon atoms; alkenyl having 2 to 12 about carbon atoms; alkynyl having 2 to 12 about carbon atoms; alkoxy having 1 to about 12 carbon atoms; alkylthio having 1 to about 12 carbon atoms; alkylsulfinyl having 1 to about 12 carbon atoms; alkylsulfonyl having 1 to about 12 carbon atoms; alkylamino having 1 to about 12 carbon atoms; benzyl; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic; and Z is hydrogen.

6. The compound of claim 2 wherein R and/or R^2 is selected from the group consisting of t-butyl; chloro-t-butyl; (dimethylamino)-t-butyl; propionate; piperidinoethyl; formyloxy; acetoxy; propionyloxy; phenylcarbonyloxy; benzylcarbonyloxy; piperidino; amino; diethylamino; dipropylamino;

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acetylcarbonyloxy; propionylcarbonyloxy; phenylcarbonyloxy; benzylcarbonyloxy; dimethylaminocarbonyloxy; cyclopentylcarbonyloxy; cyclobutylcarbonyloxy; cyclohexylcarbonyloxy; cycloheptylcarbonyloxy; and Z is hydrogen.

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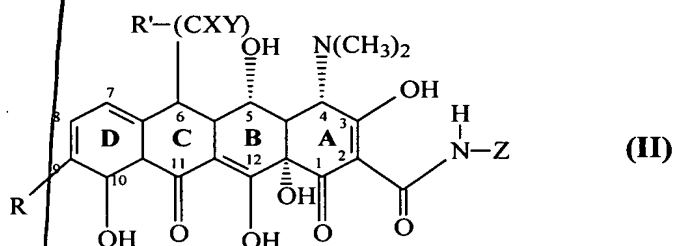
The compound of claim 1, wherein said compound is selected from the group consisting of 5-propionate-9-t-butyl doxycycline; 9-t-butyl-6-deoxy-5-propionylcarbonyloxytetracycline, 9-t-butyl-6-deoxy-5-acetylcarbonyloxytetracycline, 9-t-butyl-6-deoxy-5-cyclobutylcarbonyloxytetracycline, and pharmaceutically acceptable salts thereof.

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8. A 9,13-substituted tetracycline compound.

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9. A compound of claim 8 that is of the following Formula II:



wherein R is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

R¹ is hydrogen, hydroxy, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

X and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or heteroaromatic group; and pharmaceutically acceptable salts thereof.

10. A compound of claim 8 that is:

13-cyclopentylthio-9-t-butyl-5-oxy-tetracycline;

13-methylthio-9-t-butyl-5-oxy-tetracycline;

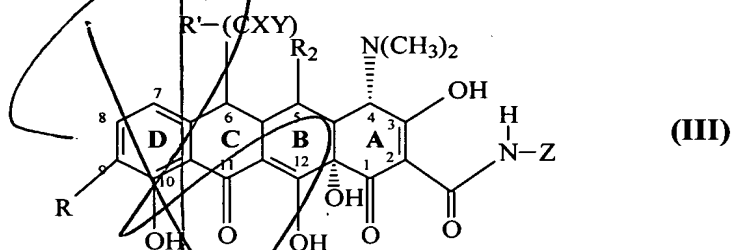
13-ethylthio-9-t-butyl-5-oxy-tetracycline;

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- 13-propylthio-9-t-butyl-5-oxy-tetracycline;
 13-isopropylthio-9-t-butyl-5-oxy-tetracycline;
 13-butylthio-9-t-butyl-5-oxy-tetracycline;
 13-isobutylthio-9-t-butyl-5-oxy-tetracycline;
 5 13-pentylthio-9-t-butyl-5-oxy-tetracycline;
 13-isopentylthio-9-t-butyl-5-oxy-tetracycline;
 13-cyclobutylthio-9-t-butyl-5-oxy-tetracycline;
 13-cyclopentylthio-9-t-butyl-5-oxy-tetracycline;
 13-cyclohexylthio-9-t-butyl-5-oxy-tetracycline;
 10 13-phenylthio-9-t-butyl-5-oxy-tetracycline;
 13-(3,4-dichlorophenyl)thio-9-t-butyl-5-oxy-tetracycline;
 13-benzylthio-9-t-butyl-5-oxy-tetracycline;
 13-(4-chlorobenzyl)thio-9-t-butyl-5-oxy-tetracycline;
 13-(3,4-dichlorobenzyl)thio-9-t-butyl-5-oxy-tetracycline;
 15 13-(4-methoxybenzyl)thio-9-t-butyl-5-oxy-tetracycline;
 13-(2,3-dihydroxypropyl)thio-9-t-butyl-5-oxy-tetracycline; and
 5-propionate-13-cyclopentylthio-9-t-butyl oxytetracycline;
 5-propionate-13-cyclopentylthio-9-piperidinoethyl oxytetracycline;
 and pharmaceutically acceptable salts thereof.

11. A 5,9,13-substituted tetracycline.
12. A compound of claim 11 that is of the following Formula III:



25 wherein R is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;
 R² is alkanoyl; aroyl; alkaroyl; carbocyclic aryl, heteroaromatic, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl such as benzyl;

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X and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an aryalkyl;

Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or heteroaromatic group; and pharmaceutically acceptable salts thereof.

13. A compound of claim 11 that is:

13-cyclopentylthio-9-t-butyl-5-formyloxy-tetracycline;

13-methylthio-9-t-butyl-5-acetoxy-tetracycline;

13-ethylthio-9-t-butyl-5-propionylcarbonyloxy-tetracycline;

13-propylthio-9-t-butyl-5-butanylcarbonyloxy-tetracycline;

13-isopropylthio-9-t-butyl-5-cyclopentylcarbonyloxy-tetracycline;

13-butylthio-9-t-butyl-5-cyclohexylcarbonyloxy-tetracycline;

13-isobutylthio-9-t-butyl-5-cycloheptylcarbonyloxy-tetracycline;

13-pentylthio-9-t-butyl-5-formyloxy-tetracycline;

13-isopentylthio-9-t-butyl-5-acetoxy-tetracycline;

13-cyclobutylthio-9-t-butyl-5-propionylcarbonyloxy-tetracycline;

13-cyclopentylthio-9-t-butyl-5-cyclopentanylcarbonyloxy-tetracycline;

13-cyclohexylthio-9-t-butyl-5-cyclohexylcarbonyloxy-tetracycline;

13-phenylthio-9-t-butyl-5-phenylacetylcarbonyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-formyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-acetoxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-propionylcarbonyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-phenylcarbonyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-benzylcarbonyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-dimethylamino carbonyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclopentyl carbonyloxy-tetracycline;

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cyclobutyl carbonyloxy-tetracycline;

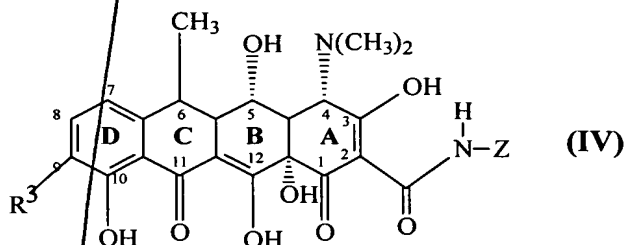
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13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-S-cyclohexyl
carbonyloxy-tetracycline; or

13-cyclopentylthio-9-[(dimethylamino)-t-butyl]-6-alpha-deoxy-5-cycloheptyl
carbonyloxy-tetracycline; and pharmaceutically acceptable salts thereof.

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14. A compound of the following Formula IV:



wherein R^3 is alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
alkylsulfonyl; alkylamino; or an aryalkyl;

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Z is hydrogen, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl;
alkylsulfonyl; alkylamino; aryalkyl, carbocyclic aryl, heteroalicyclic or
heteroaromatic group; and pharmaceutically acceptable salts thereof.

15. A compound of claim 14 which is

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9-t-butyl tetracycline;

9-t-butyl anhydrotetracycline;

9-t-butyl minocycline; and pharmaceutically acceptable salts thereof.

16. The compound of claim 14 wherein R^3 is alkyl having 1 to about 20 carbon
atoms; alkenyl having 2 to about 20 carbon atoms; alkynyl having 2 to about 20
carbon atoms; alkoxy having 1 to about 20 carbon atoms; alkylthio having 1 to
about 20 carbon atoms; alkylsulfinyl having from 1 to about 20 carbon atoms;
alkylsulfonyl having from 1 to about 20 carbon atoms; alkylamino having from 1
to about 20 carbon atoms; or aryalkyl; and

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Z is hydrogen, alkyl having 1 to about 20 carbon atoms; alkenyl having 2
to about 20 carbon atoms; alkynyl 2 to about 20 carbon atoms; alkoxy 1 to about
20 carbon atoms; alkylthio having 1 to about 20 carbon atoms; alkylsulfinyl
having from 1 to about 20 carbon atoms; alkylsulfonyl having from 1 to about 20
carbon atoms; alkylamino having from 1 to about 20 carbon atoms; aryalkyl;
carbocyclic aryl, or an heteroalicyclic group.

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17. The compound of claim 14 wherein R^3 is alkyl having 1 to about 12 carbon atoms; alkenyl having 2 to 12 about carbon atoms; alkynyl having 2 to 12 about carbon atoms; alkoxy having 1 to about 12 carbon atoms; alkylthio having 1 to about 12 carbon atoms; alkylsulfinyl having 1 to about 12 carbon atoms; alkylsulfonyl having 1 to about 12 carbon atoms; alkylamino having 1 to about 12 carbon atoms; or benzyl; and Z is hydrogen.
18. The compound of claim 14 wherein R^3 is selected from the group consisting of t-butyl; chloro-t-butyl; (dimethylamino)-t-butyl; methylcyclohexyl; methylcyclobutyl; methylpentyl; bromomethylpentyl; nitromethylpentyl; and acetoxymethylpentyl.
19. The compound of claim 14, wherein said compound is selected from the group consisting of 9-t-butyl-6-deoxy-5-hydroxytetracycline, 9-[1'-(1'-methyl)cyclohexyl]-6-deoxy-5-hydroxytetracycline, 9-[1'-(1'-methyl)cyclopentyl]-6-deoxy-5-hydroxytetracycline, 9-[1'-(1'-methyl)cyclobutyl]-6-deoxy-5-hydroxytetracycline, 9-[2'-(2'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-bromo-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-dimethylamino-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-pyrrolidinyl-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-cyano-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-nitro-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline, 9-[4'-(1'-acetoxymethyl-4'-methyl)pentyl]-6-deoxy-5-hydroxytetracycline); 9-t-butyl tetracycline; 9-t-butyl anhydrotetracycline; 9-t-butyl minocycline; and pharmaceutically acceptable salts thereof.
20. A method for treating against a targeted microorganism comprising administering to the microorganism a compound of any one of claims 1 through 19.
21. A method for treating against bacteria comprising administering to the bacteria a compound of any one of claims 1 through 19.
22. A method for treating a mammal suffering from or susceptible to a microorganism infection or disease associated therewith comprising administering to the mammal a compound of any one of claims 1 through 19.

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23. A method for treating a mammal suffering from or susceptible to bacteria infection comprising administering to the mammal a compound of any one of claims 1 through 19.
- 5 24. The method of claim 22 or 23 wherein the mammal is a human.
25. The method of any one of claims 20-22 wherein the microorganism or bacteria is tetracycline sensitive.
- 10 26. The method of any one of claims 20-22 wherein the microorganism or bacteria is tetracycline resistant.
27. The method of any one of claims 20-26 wherein the bacteria is *E. coli.*, *S. aureus* or *E. faecalis*.
- 15 28. A method for converting tetracycline resistant bacteria into tetracycline resistant bacteria, comprising
 - a) contacting the resistant bacteria with a predetermined quantity of a compound of any one of claims 1 through 11, and
 - 20 b) concomitantly administering to the bacteria a predetermined quantity of a tetracycline-type compound that is different than the compound of step a).
29. A pharmaceutical composition of any one of claims 1 through 19.

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